

10573280

File 5:Biosis Previews(R) 1926-2008/Aug W1  
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Set	Items	Description
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? s ((islet or pancrea?) (3w)glucose()6()phosphatase)	28799	ISLET
	309045	PANCREA?
	359709	GLUCOSE
	2065310	6
	28	PHOSPHATASE
S1	0	((ISLET OR PANCREA?) (3W)GLUCOSE()6()PHOSPHATASE)
? s ((islet or pancrea?) (3w)glucose()6()phosphatase)	>>>Help is not available for S1	
? s ((islet or pancrea?) (3w)glucose()6()phosphatase)	28799	ISLET
	309045	PANCREA?
	359709	GLUCOSE
	2065310	6
	135574	PHOSPHATASE
S2	70	((ISLET OR PANCREA?) (3W)GLUCOSE()6()PHOSPHATASE)
? s s2 and (autoantibod? or auto()antibod?)	70	S2
	31073	AUTOANTIBOD?
	51752	AUTO
	679398	ANTIBOD?
	4713	AUTO(W)ANTIBOD?
S3	4	S2 AND (AUTOANTIBOD? OR AUTO()ANTIBOD?)
? t s3/7/1-4		

3/7/1

DIALOG(R)File 5:Biosis Previews(R)  
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0020381031 BIOSIS NO.: 200800427970  
The frequency and immunodominance of islet-specific CD8(+) T-cell responses  
change after type 1 diabetes diagnosis and treatment  
AUTHOR: Martinuzzi Emanuelu; Novelli Giulia; SCotto Matthieu; Blancou  
Philippe; Bach Jean-Marie; Chaillous Lucy; Bruno Graziella; Chatenoud  
Lucienne; van Endert Peter; Mallone Roberto (Reprint)  
AUTHOR ADDRESS: Hop St Vincent de Paul, INSERM U561, 82 Ave Denfert,  
F-75674 Paris, France\*\*France  
AUTHOR E-MAIL ADDRESS: roberto.mallone@inserm.fr  
JOURNAL: Diabetes 57 (5): p1312-1320 MAY 2008 2008  
ITEM IDENTIFIER: doi:10.2337/db07-1594  
ISSN: 0012-1797  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: OBJECTIVE-Islet-reactive CD8(+) T-cells play a key role in the  
pathogenesis of type 1 diabetes in the NOD mouse. The predominant T-cell  
specificities change over time, but whether similar shifts also occur  
after clinical diagnosis and insulin treatment in type 1 diabetic  
patients is unknown. RESEARCH DESIGN AND METHODS-We took advantage of a

recently validated islet-specific CD8(+) T-cell gamma-interferon enzyme-linked immunospot (lSL8Spot) assay to follow responses against preproinsulin (PPI), GAD, insulinoma-associated protein 2 (IA-2), and %islet%%-specific %glucose%%-%%6%%-%phosphatase%% catalytic subunit-related protein (IGRP) epitopes in 15 HLA-A2(+) adult type 1 diabetic patients close to diagnosis and at a second time point 7-16 months later. RESULTS-CD8(+) T-cell reactivities were less frequent at follow-up, as 28.6% of responses tested positive at type 1 diabetes diagnosis vs. 13.2% after a median of 11 months (P = 0.003). While GAD and IA-2 %autoantibody%% (aAb) titers were unchanged in 75% of cases, the fraction of patients responding to PPI and/or GAD epitopes by lSL8Spot decreased from 60-67 to 20% (P < 0.02). The previously subdominant IA-2(206-214) and IGRP(265-273) peptides were newly targeted, thus becoming the immunodominant epitopes. CONCLUSIONS-Shifts both in frequency and in immunodominance of CD8(+) T-cell responses occur more rapidly than do changes in aAb titers. These different kinetics may suggest complementary clinical applications for T-cell and aAb measurements.

3/7/2

DIALOG(R)File 5:Biosis Previews(R)  
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0020079939 BIOSIS NO.: 200800126878  
A bioinformatic approach to identification of novel type 1 diabetes autoantigens  
AUTHOR: Hutton J C (Reprint); Wenzlau J M; Juhl K; Sarkar S; Yu L; Eisenbarth G S; Jensen J; Davidson H W  
AUTHOR ADDRESS: Univ Colorado, Hlth Sci Ctr, Barbara Davis Ctr Childhood Diabet, Aurora, CO USA\*\*USA  
JOURNAL: Diabetologia 50 (Suppl. 1): pS63 SEP 2007 2007  
CONFERENCE/MEETING: 43rd Annual Meeting of the European-Association-for-the-Study-of-Diabetes Amsterdam, NETHERLANDS September 18 -21, 2007; 20070918  
SPONSOR: European Assoc Study Diabet  
ISSN: 0012-186X  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Citation  
LANGUAGE: English

3/7/3

DIALOG(R)File 5:Biosis Previews(R)  
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19083084 BIOSIS NO.: 200600428479  
Alternative splicing of G6PC2, the gene coding for the %islet%%-specific %glucose%%-%%6%%-%phosphatase%% catalytic subunit-related protein (IGRP), results in differential expression in human thymus and spleen compared with pancreas  
AUTHOR: Dogra R S (Reprint); Vaidyanathan P; Prabakar K R; Marshall K E; Hutton J C; Pugliese A  
AUTHOR ADDRESS: Univ Miami, Diabet Res Inst, Immunogenet Program, 1450 NW 10th Ave, Miami, FL 33136 USA\*\*USA  
AUTHOR E-MAIL ADDRESS: APuglies@med.miami.edu  
JOURNAL: Diabetologia 49 (5): p953-957 MAY 2006 2006

ISSN: 0012-186X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** Autoimmunity to insulin, glutamic acid decarboxylase and the tyrosine-phosphatase-like protein IA-2 is associated with type 1 diabetes. The production of self-molecules in thymus and secondary lymphoid tissues is critical for self-tolerance; reduced levels may impair tolerance and predispose to autoimmunity, as shown for insulin. Alternative splicing causes differential expression of IA-2 gene (PTPRN) transcripts and IA-2 protein in human thymus and spleen compared with pancreas. IA-2 sequences not present in lymphoid tissues become autoimmune targets in type 1 diabetes. The beta cell molecule %%%islet%%% -specific %%%glucose%%%-%%%6%%%-%%%phosphatase%%% catalytic subunit-related protein (IGRP) is an autoantigen in the non-obese diabetic (NOD) mouse, a model of type 1 diabetes. IGRP is a candidate autoantigen in the human disease, but robust assays for IGRP %%%autoantibodies%%% and/or autoreactive T cells are not available. Both full-length and IGRP splice variants encoded by the G6PC2 gene are expressed in the pancreas. In this study we tested the hypothesis that IGRP splice variants could be differentially expressed in thymus and spleen compared with the pancreas. We evaluated the expression of G6PC2 transcripts in matched human thymus, spleen and pancreas specimens by RT-PCR. Alternative splicing results in differential expression of G6PC2 transcripts in thymus and spleen compared with pancreas. The full-length transcript is expressed in human pancreas but not in thymus or spleen. Five alternative spliced forms are always expressed in pancreas but those lacking exons 2, 3 and 4, alone or in combination, were rarely detected in thymus or spleen. Conclusions/interpretation: Differential tissue expression might favour autoimmune responses to IGRP in humans; target epitopes may be encoded by exons 3 and 4, or at the junctions of the conserved exons in the spliced transcripts. This information may aid in designing synthetic peptides for the identification of IGRP-specific autoreactive T cells in patients with type 1 diabetes.

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DIALOG(R)File 5:Biosis Previews(R)  
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17524108 BIOSIS NO.: 200300478063  
A pancreatic beta-cell-specific homolog of glucose-6-phosphatase emerges as a major target of cell-mediated autoimmunity in diabetes.  
AUTHOR: Hutton John C (Reprint); Eisenbarth George S  
AUTHOR ADDRESS: Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, 4200 East 9th Avenue, Denver, CO, 80262, USA\*\*USA  
AUTHOR E-MAIL ADDRESS: john.hutton@uchsc.edu  
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 100 (15): p8626-8628 July 22, 2003 2003  
MEDIUM: print  
ISSN: 0027-8424 \_(ISSN print)  
DOCUMENT TYPE: Article  
RECORD TYPE: Citation  
LANGUAGE: English  
? s sl and diabetes and diagnose

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>>>Term "ANDD" in invalid position
? s s2 and diabetes and diagnose
    70 S2
    234696 DIABETES
    15812 DIAGNOSE
    S4      0 S2 AND DIABETES AND DIAGNOSE
? ds

Set    Items    Description
S1      0 ((ISLET OR PANCREA?) (3W)GLUCOSE()6()PHOSPHATASE)
S2      70 ((ISLET OR PANCREA?) (3W)GLUCOSE()6()PHOSPHATASE)
S3      4 S2 AND (AUTOANTIBOD? OR AUTO()ANTIBOD?)
S4      0 S2 AND DIABETES AND DIAGNOSE
? s (glucose()6()phosphatase) and diabetes
    359709 GLUCOSE
    2065310 6
    135574 PHOSPHATASE
    5910 GLUCOSE(W)6(W)PHOSPHATASE
    234696 DIABETES
    S5      472 (GLUCOSE()6()PHOSPHATASE) AND DIABETES
? s s5 and antibod?
    472 S5
    679398 ANTIBOD?
    S6      10 S5 AND ANTIBOD?
? t s6/7/1-10
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6/7/1  
DIALOG(R)File 5:Biosis Previews(R)  
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0019587710 BIOSIS NO.: 200700247451  
CD8(+) T-cell responses identify beta-cell autoimmunity in human type 1  
%%%diabetes%%%  
AUTHOR: Mallone Roberto (Reprint); Martinuzzi Emanuela; Blancou Philippe;  
Novelli Giulia; Afonso Georgia; Dolz Manuel; Bruno Graziella; Chaillous  
Lucy; Chatenoud Lucienne; Bach Jean-Marie; van Endert Peter  
AUTHOR ADDRESS: Hop Necker Enfants Malad, INSERM U580, 161 Rue Sevres,  
F-75743 Paris, France\*\*France  
AUTHOR E-MAIL ADDRESS: mallone@necker.fr; vanendert@necker.fr  
JOURNAL: Diabetes 56 (3): p613-621 MAR 2007 2007  
ISSN: 0012-1797  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Despite the understanding that type I %%%diabetes%%% pathogenesis is mediated by T-cells, detection of these rare lymphocytes remains largely elusive. Suitable T-cell assays are highly needed, since they could offer preclinical diagnoses and immune surrogate end points for clinical trials. Although CD4(+) T-cell assays have met with limited success, CD8(+) T-cells are increasingly recognized as key actors in the %%%diabetes%%% of the NOD mouse. CDS+ T-cells are likely to play a role also in humans and may provide new markers of beta-cell autoimmunity. Taking advantage of a panel of HLA-A2-restricted beta-cell epitopes derived from preproinsulin, GAD, and islet %%%glucose%%%-%%%6%%%-%%%phosphatase%%% catalytic subunit-related protein (IGRP), we have implemented an islet-specific CD8(+) T-cell interferon-gamma

enzyme-linked immunospot (ISL8Spot) assay. The ISL8Spot assay is capable of detecting and quantifying P-cell-reactive CD8(+) T-cells directly ex vivo, without any preliminary expansion, using either fresh or frozen samples. Positive ISL8Spot responses separate new-onset diabetic and healthy samples with high accuracy (86% sensitivity, 91% specificity), using as few as five immunodominant epitopes. Moreover, sensitivity reaches 100% when the ISL8Spot assay is complemented by %%%antibody%%% determinations. Combination of CD8(+) T-cell measurements with immune intervention strategies may open new avenues toward type 1 %%%diabetes%%% prediction and prevention.

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19326180 BIOSIS NO.: 200600671575

Identification of novel HLA-A\*0201-restricted epitopes in recent-onset type 1 diabetic subjects and %%%antibody%%%-positive relatives

AUTHOR: Standifer Nathan E (Reprint); Qin Ouyang; Panagiotopoulos Constadina; Verchere C Bruce; Tan Rusung; Greenbaum Carla J; Pihoker Catherine; Nepom Gerald T

AUTHOR ADDRESS: Virginia Mason, Benaroya Res Inst, 1201 9th Ave, Room 260, Seattle, WA 98101 USA\*\*USA

AUTHOR E-MAIL ADDRESS: nstand@benaroyaresearch.org

JOURNAL: Diabetes 55 (11): p3061-3067 NOV 2006 2006

ISSN: 0012-1797

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** Cytotoxic T-lymphocytes (CTLs) are considered to be essential for beta-cell destruction in type I %%%diabetes%%%. However, few islet-associated peptides have been demonstrated to activate autoreactive CTLs from type I diabetic subjects. In an effort to identify novel epitopes, we used matrix-assisted algorithms to predict peptides of glial fibrillary acidic protein (GFAP), prepro-islet amyloid polypeptide (ppIAPP), and islet-specific %%%glucose%%%-%%6%%-%%%phosphatase%%% catalytic subunit-related protein (IGRP) that likely bind to HLA-A\*0201 with a strong affinity and contain a COOH-terminal proteasomal cleavage site. Seven peptides stabilized HLA-A\*0201 expression in binding assays and were used to stimulate peripheral blood mononuclear cells and were evaluated for granzyme B secretion. We found that 5 of 13 type 1 diabetic subjects and 4 of 6 %%%antibody%%%-positive relatives exhibited greater numbers of granzyme B-secreting cells in response to at least one putative epitope compared with healthy control subjects. The most prevalent responses in %%%antibody%%%-positive and type 1 diabetic subjects were to ppIAPP(9-17). Other peptides recognized by type I diabetic or %%%antibody%%%-positive subjects included GFAP(143-151), IGRP(152-160), and GFAP(214-222). These data implicate peptides of ppIAPP, GFAP, and IGRP as CTL epitopes for a heterogenous CD8(+) T-cell response in type 1 subjects and %%%antibody%%%-positive relatives.

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19324735 BIOSIS NO.: 200600670130  
Epitopes from IGRP recognised by CD4 T cells in diabetic NOD mice  
AUTHOR: Yang Tao (Reprint); Davidson Howard W; Hutton John C  
AUTHOR ADDRESS: Aurora, CO USA\*\*USA  
JOURNAL: Diabetes 55 (Suppl. 1): pA278 JUN 2006 2006  
CONFERENCE/MEETING: 66th Annual Meeting of the  
American-Diabetes-Association Washington, DC, USA June 09 -13, 2006;  
20060609  
SPONSOR: Amer Diabet Assoc  
ISSN: 0012-1797  
DOCUMENT TYPE: Meeting; Meeting Poster  
RECORD TYPE: Citation  
LANGUAGE: English

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DIALOG(R)File 5:Biosis Previews(R)  
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19019308 BIOSIS NO.: 200600364703  
Proinsulin precedes IGRP in the hierarchy of autoantigens in autoimmune  
%%%diabetes%%%  
AUTHOR: Krishnamurthy B (Reprint); Dudek N L; Thomas H E; Purcell A W; Lew  
A M; Harrison L C; Kay T W H  
AUTHOR ADDRESS: St Vincents Inst Med Res, Fitzroy, Vic 3065, Australia\*\*  
Australia  
JOURNAL: Tissue Antigens 66 (5): p467-468 NOV 2005 2005  
CONFERENCE/MEETING: 35th Annual Scientific Meeting of the  
Australasian-Society-for-Immunology/14th International HLA and  
Immunogenetics Workshops Melbourne, AUSTRALIA November 29 -December 02,  
2005; 20051129  
SPONSOR: Australasian Soc Immunol  
ISSN: 0001-2815  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Citation  
LANGUAGE: English

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DIALOG(R)File 5:Biosis Previews(R)  
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18991103 BIOSIS NO.: 200600336498  
Elevated O-GlcNAc cycling on FOXO1A mediates inappropriate hepatic  
gluconeogenesis  
AUTHOR: Housley Michael Patrick (Reprint); Rodgers Joseph Thomas;  
Puigserver Pere; Hart Gerald Warren  
AUTHOR ADDRESS: Johns Hopkins Sch Med, Baltimore, MD 21205 USA\*\*USA  
JOURNAL: FASEB Journal 20 (5, Part 2): pA955 MAR 7 2006 2006  
CONFERENCE/MEETING: Experimental Biology 2006 Meeting San Francisco, CA,  
USA April 01 -05, 2006; 20060401  
SPONSOR: Amer Assoc Anatomists  
Amer Physiol Soc  
Amer Soc Biochem & Mol Biol  
Amer Soc Investigat Pathol  
Amer Soc Nutr

Amer Soc Pharmacol & Expt Therapeut  
ISSN: 0892-6638  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** Hepatic gluconeogenesis, which is normally suppressed by insulin, is abnormally activated in %%%diabetes%%%. The transcription factor FOXO1A controls expression of the gluconeogenic enzymes, PEPCK and %%%Glucose6-Phosphatase%%% Phosphatase%%% . Insulin signaling results in the nuclear exclusion of FOXO1A but post-translational regulation of transactivation within the nucleus also occurs. Dynamic Modification of proteins by O-GlcNAc serves as a nutrient and stress sensor and is often competitive with phosphorylation. Anti-O-GlcNAc %%%antibodies%%% and lectin studies have shown that FOXO1A is O-GlcNAcylated. Increased flux into the UDP-GlcNAc (donor for O-GlcNAcylation) synthesis pathway increases FOXO1A transcriptional activity in an O-GlcNAc transferase (OGT) dependent manner. Hyperglycemia increases O-GlcNAcylation of FOXO1A in hepatoma cells and this increase is reversed by insulin. We conclude that hyperglycemia increases the O-GlcNAc modification of FOXO1A resulting in paradoxically elevated hepatic gluconeogenesis, further exacerbating glucose toxicity in %%%diabetes%%%.

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17527704 BIOSIS NO.: 200300496423  
Human %%%glucose%%%-%%%6%%%-%%%phosphatase%%% molecules and uses thereof  
AUTHOR: Chen Hong (Reprint)  
JOURNAL: Official Gazette of the United States Patent and Trademark Office  
Patents 1274 (5): Sep. 30, 2003 2003  
MEDIUM: e-file  
ISSN: 0098-1133 \_(ISSN print)  
DOCUMENT TYPE: Patent  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** The invention provides isolated nucleic acids encoding human pancreatic islet-specific %%%glucose%%%-%%%6%%%-%%%phosphatase%%% proteins and nucleic acids having diagnostic, preventive, therapeutic, and other uses. These nucleic acids and proteins are useful for diagnosis, prevention, and therapy of a number of human and other animal disorders. The invention also provides antisense nucleic acid molecules, expression vectors containing the nucleic acid molecules of the invention, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a nucleic acid molecule of the invention has been introduced or disrupted. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides, and %%%antibodies%%% . Diagnostic, screening, and therapeutic methods utilizing compositions of the invention are also provided. The nucleic acids and polypeptides of the present invention are useful as modulating agents in regulating a variety of cellular processes, including those which are aberrant in %%%diabetes%%% and other disorders associated with pancreatic dysfunction.

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DIALOG(R)File 5:Biosis Previews(R)  
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17516912 BIOSIS NO.: 200300485631  
Human %%glucose%%-%%6%%-%%phosphatase%% molecules and uses thereof  
AUTHOR: Chen Hong (Reprint)  
AUTHOR ADDRESS: Newton, MA, USA\*\*USA  
JOURNAL: Official Gazette of the United States Patent and Trademark Office  
Patents 1274 (4): Sep. 23, 2003 2003  
MEDIUM: e-file  
ISSN: 0098-1133 \_(ISSN print)  
DOCUMENT TYPE: Patent  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: The invention provides isolated nucleic acids encoding human pancreatic islet-specific %%glucose%%-%%6%%-%%phosphatase%% proteins and nucleic acids having diagnostic, preventive, therapeutic, and other uses. These nucleic acids and proteins are useful for diagnosis, prevention, and therapy of a number of human and other animal disorders. The invention also provides antisense nucleic acid molecules, expression vectors containing the nucleic acid molecules of the invention, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a nucleic acid molecule of the invention has been introduced or disrupted. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides, and %%antibodies%%. Diagnostic, screening, and therapeutic methods utilizing compositions of the invention are also provided. The nucleic acids and polypeptides of the present invention are useful as modulating agents in regulating a variety of cellular processes, including those which are aberrant in %%diabetes%% and other disorders associated with pancreatic dysfunction. The invention includes methods of modulating secretion of pancreatic hormones such as insulin and glucagon, and these methods can be used to alleviate disorders (e.g., %%diabetes%% and hyperinsulinemia) associated with aberrant secretion of these hormones.

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DIALOG(R)File 5:Biosis Previews(R)  
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12702363 BIOSIS NO.: 199598170196  
High Levels of %%Glucose%%-%%6%%-%%Phosphatase%% Gene and Protein  
Expression Reflect an Adaptive Response in Proliferating Liver and  
%%Diabetes%%  
AUTHOR: Haber Barbara A; Chin Simon; Chuang Emil; Buikhuisen Wieneke; Naji  
Ali; Taub Rebecca (Reprint)  
AUTHOR ADDRESS: Howard Hughes Med. Inst., Dep. Genet., Univ. Pennsylvania,  
Sch. Med., Philadelphia, PA 19104-6145, USA\*\*USA  
JOURNAL: Journal of Clinical Investigation 95 (2): p832-841 1995 1995  
ISSN: 0021-9738  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** The regenerating liver after partial hepatectomy is one of the few physiologic models of cellular proliferation in the adult animal. During hepatic regeneration, the animal is able to maintain metabolic homeostasis despite the acute loss of two thirds of hepatic tissue. In examining the molecular mechanisms regulating hepatic regeneration, we isolated novel immediate-early genes that are rapidly induced as the remnant liver undergoes the transition from its normal quiescent state into the GI phase of the cell cycle. One of the most rapidly and highly induced genes which we initially termed RL-1, encodes rat %%%glucoset%%%-%%%G6Pase%%-%%%phosphatase%%% (rG6Pase). G6Pase mRNA peaks at 30 min and 36-48 h after hepatectomy correlating with the first and second rounds of cell division. This finding is compatible with studies that showed that G6Pase enzyme activity increases during liver regeneration. However, the increase in G6Pase mRNA is much more dramatic, indicating that it is a more sensitive indicator of this regulation. G6Pase gene expression peaks in the perinatal time period in the liver and remains elevated during the first month of life. The expression of the G6Pase gene is also dramatically elevated in BB diabetic rats, again higher than the enzyme elevation, and its relative induction after partial hepatectomy is blunted in these animals. Insulin treatment of partially hepatectomized diabetic animals downregulates the expression of G6Pase mRNA. Using specific %%%antibodies%%% against G6Pase, we detect a 36-kD G6Pase protein, and its level is elevated in regenerating and diabetic livers. The pattern of G6Pase mRNA expression appears to reflect similar changes in insulin and glucagon levels which accompany %%%diabetes%%% and hepatic proliferation. The elevation of G6Pase expression in these conditions is indicative of its importance as a regulator of glucose homeostasis in normal and abnormal physiologic states.

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DIALOG(R)File 5:Biosis Previews(R)  
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07757842 BIOSIS NO.: 198580066737  
METABOLIC ZONATION IN LIVER OF DIABETIC RATS ZONAL DISTRIBUTION OF  
PHOSPHOENOLPYRUVATE CARBOXYKINASE EC-4.1.1.32 PYRUVATE KINASE EC-2.7.1.40  
%%%GLUCOSE%%%-%%%G6Pase%%%-%%%PHOSPHATASE%%% EC-3.1.3.9 AND SUCCINATE  
DEHYDROGENASE EC-1.3.99.1  
AUTHOR: MIETHKE H (Reprint); WITTIG B; NATH A; ZIERZ S; JUNGERMAN K  
AUTHOR ADDRESS: INSTITUT FUER BIOCHEMIE DER UNIVERSITAET, HUMBOLDTALLEE 23,  
D-3400 GOETTINGEN\*\*WEST GERMANY  
JOURNAL: Biological Chemistry Hoppe-Seyler 366 (5): p493-502 1985  
ISSN: 0177-3593  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: ENGLISH

**ABSTRACT:** The activities and zonal distribution of key enzymes of carbohydrate metabolism were studied in livers of diabetic rats. Forty-eight hours after alloxan treatment the following alterations were observed, intermediate values being reached after 24 h. Blood glucose, acetoacetate and  $\beta$ -hydroxybutyrate were increased to more than 500%; liver glycogen was reduced to about 100%. Portal vein insulin was reduced to below 10%, portal glucagon was increased to almost 200%. The glucogenic enzymes phosphoenolpyruvate carboxykinase and %%%glucose%%%-%%%

phosphatase were enhanced to 320% and 150%, respectively. The glycolytic enzymes glucokinase and pyruvate kinase L (differentiated from the M2 isoenzyme with a specific anti-L-antibody) were lowered to 50% and 75%, respectively. The citrate cycle enzyme succinate dehydrogenase remained unchanged. The normal perivenous gradient of phosphoenolpyruvate carboxykinase of about 3:1, as measured in microdissected tissue samples, was enhanced to about 4:1 with activities elevated to 230% and 190%, respectively, in the 2 zones. The normal periportal to perivenous gradient of pyruvate kinase L of about 1:1.7, as determined with the microdissection technique, was reduced to about 1:1.4 with levels lowered to 55% and 45%, respectively, in the 2 zones. The even zonal distribution of pyruvate kinase M2 remained unaltered. The normal periportal to perivenous gradients of glucose and phosphate, demonstrated histochemically, remained unaffected. In insulin-deficient diabetes the gluconeogenic capacity was strongly elevated in the periportal zone while the glycolytic capacity was reduced in the perivenous area. Apparently in diabetes, in contrast to starvation, the glucostat function of the liver and the concomitant reciprocal distribution of glucogenic and glycolytic enzymes is not lost, but only impaired due to shifts of the zonal enzyme levels.

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0001669023 BIOSIS NO.: 19664700073125

## The ontogenesis of the endocrine pancreas and carbohydrate metabolism

BOOK TITLE: International Conference on organogenesis, Baltimore, Maryland,  
6-12 September, 1964

5-12 September, 1964

AUTHOR: GRIEVE T ADESANMI T  
AUTHOR ADDRESS: Dept. Anat. Univ. Ibadan, Ibadan, Nigeria

**AUTHOR ADDRESS:**

BOOK PUBLISHER: Holt, Rinehart and Winston, New York

BOOK PUBLISHER: H&I  
DOCUMENT TYPE: Book

DOCUMENT TYPE: Book

RECORD TYPE: Abstract

LANGUAGE: Unspecified

**ABSTRACT:** The results of the investigations discussed strongly indicate that the embryonic endocrine pancreas is capable of producing insulin and glucagon. In some species, both insulin and glucagon were detected biochemically in extracts of fetal pancreas before the specific granules could be observed cytologically. Insulin was also detected during development by the fluorescent  $\text{^{125}I}$ antibody method. Pancreatic islets have been grown successfully in vitro. Cells of these islets, grown in organ culture, were observed to have  $\{\beta\}$  granules. If  $\{\beta\}$  granulation can be used as evidence of insulin formation, then it may be said that pancreatic islets are capable of self-differentiation in vitro. Enzyme histochemistry of the embryonic pancreas revealed the presence of oxidative enzymes which are important in glucose metabolism. The presence of these enzymes and of  $\text{^{125}I}$ glucose- $\text{^{32}P}$  phosphatase suggests that embryonic islets are capable of producing and secreting hormones in response to changes in blood glucose levels. Further proof of the secretion of insulin in the embryo has been obtained by the detection of the hormone in the blood of chick embryos. That the secreted hormones can produce effects on their target organs was proved by the demonstration,

in the tissues, of the presence of enzymes directly connected with glycogen metabolism, namely, phosphorylase and UDPG-glycogen synthetase. There appears to be a correlation in the appearance of enzymes in embryonic tissues and the secretion of the pancreatic hormones. Moreover, embryonic tissues have been shown to respond to pancreatic hormones. Thus, insulin increases the glycogen content of embryonic liver while glu-cagon produces glycogenolysis. Finally, embryonic pancreatic islets can respond to alterations in maternal blood sugar levels. Thus, fetal islets become hyperplastic and degranulated in response to maternal %diabetes%. ABSTRACT AUTHORS: Author

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Set	Items	Description
S1	0	((ISLET OR PANCREA?) (3W)GLUCOSE()6()PHOSPHATASE)
S2	70	((ISLET OR PANCREA?) (3W)GLUCOSE()6()PHOSPHATASE)
S3	4	S2 AND (AUTOANTIBOD? OR AUTO()ANTIBOD?)
S4	0	S2 AND DIABETES AND DIAGNOSE
S5	472	(GLUCOSE()6()PHOSPHATASE) AND DIABETES
S6	10	S5 AND ANTIBOD?

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$34.16  14 Type(s) in Format  7
$34.16  14 Types
$48.19  Estimated cost File5
$2.93   TELNET
$51.12  Estimated cost this search
$51.12  Estimated total session cost  2.661 DialUnits
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